CLAIMS

1. A compound of general formula (I):

5 in which:

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 R^1 may be (C₆ or C₁₀) aryl, (C₆ or C₁₀) arylalkyl, (C₆ or C₁₀) heteroaryl, (C₃-C₈) heterocycloalkenyl, (C₅-C₈) cycloalkene ring, (C₅-C₈) cycloalkyl, (C₅-C₈) heterocycloalkyl or a combination thereof to form a linked or fused ring system, the cyclic moiety being optionally substituted with (C₁-C₁₀) alkyl, (C₁-C₁₀) alkenyl, (C₁-C₁₀) alkynyl, (C₁-C₁₀) alkoxy, (C₁-C₁₀) thioalkoxy, hydroxyl, hydroxyl, (C₁-C₁₀) hydroxylalkyl, halo, (C₁-C₁₀) haloalkyl, amino, amido, (C₁-C₁₀) alkylamino, (C₁-C₁₀) alkylcarbonyloxy, (C₁-C₁₀) alkoxycarbonyl, (C₁-C₁₀) alkylcarbonyl, (C₁-C₁₀) alkylsulfinyl, or (C₁-C₁₀) alkylsulfonyl,

 R^2 and R^3 may each independently be hydrogen, (C₁-C₁₂) alkyl, substituted (C₁-C₁₂) alkyl, or unsaturated (C₁-C₁₂) comprising one or more C=C bond or C ≡€ bond, (C₆ or C₁₀) aryl or (C₆ or C₁₀) heteroaryl, or a combination thereof to form a linked or fused ring system, or (C_1-C_{10}) alkyl, (C_1-C_{10}) alkenyl, (C_1-C_{10}) alkynyl, (C_1-C_{10}) alkoxy, (C₁-C₁₀) thioalkoxy, hydroxyl, hydroxyl, (C₁-C₁₀) hydroxylalkyl, halo; (C₁-C₁₀) haloalkyl, cyano, nitro, amino, amido, (C_1-C_{10}) alkylamino, (C_1-C_{10}) alkylcarbonyloxy, (C_1-C_{10}) alkoxycarbonyl, (C_1-C_{10}) alkylcarbonyl, (C_1-C_{10}) alkylthiocarbonyl, (C₁-C₁₀) alkylsulfonylamino, aminosulfonyl, (C₁-C₁₀) alkylsulfinyl, or (C_1-C_{10}) alkylsulfonyl, in which the saturated or an unsaturated hydrocarbon chain is optionally interrupted by O, S, NR, CO, C(NR), N(R)SO₂, SO₂N(R), N(R)C(O)O, OC(O)N(R), N(R)C(O)N(R), OC(O), C(O)O, OSO₂, SO₂O, or OC(O)O, where R may be independently hydrogen, (C_1-C_{10}) alkyl, (C_1-C_{10}) alkenyl, (C_1-C_{10}) alkynyl, (C_1-C_{10}) alkoxy, (C_1-C_{10}) hydroxylalkyl, hydroxyl, (C_1-C_{10}) halolalkyl, where each of the saturated or unsaturated hydrocarbon chains may be optionally substituted with (C_1-C_{10}) alkyl, (C_1-C_{10}) alkenyl, (C_1-C_{10}) alkynyl, (C_1-C_{10}) alkoxy, hydroxyl, hydroxyl, (C_1-C_{10}) hydroxylalkyl, halo, (C_1-C_{10}) haloalkyl, amino, (C_1-C_{10}) alkylcarbonyloxy, (C_1-C_{10}) alkoxycarbonyl, (C_1-C_{10}) alkylcarbonyl, (C_1-C_{10}) alkylsulfonylamino, aminosulfonyl, or (C_1-C_{10}) alkylsulfonyl,

or R² and R³ optionally form a (C₆ or C₁₀) aryl, (C₆ or C₁₀) arylalkyl, (C₆ or C₁₀)

heteroaryl, (C₃-C₈) heterocycloalkenyl, (C₅-C₈) cycloalkene ring, (C₅-C₈) cycloalkyl,

(C₅-C₈) heterocycloalkyl linked or fused ring system, optionally containing up to 3 heteroatoms, e.g. oxygen, nitrogen, sulphur or phosphorous.

or R¹ and R² optionally form a (C₆ or C₁₀) aryl, (C₆ or C₁₀) arylalkyl, (C₆ or C₁₀)

heteroaryl, (C₃-C₈) heterocycloalkenyl, (C₅-C₈) cycloalkene ring, (C₅-C₈) cycloalkyl,

(C₅-C₈) heterocycloalkyl linked or fused ring system, optionally the ring formed may be further substituted with a group R¹ as defined above, or the ring formed may be fused to a further C₆ aryl group which may be optionally substituted with a group R¹ as defined above, or a group R¹R²N, with R¹ and R² as defined above,

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n may be equal to 0, 1 or 2,

X may be hydroxyl (-OH), -OR, NHR, hydroxamate (-NHOH), NHOR, NROR, NRNHR, or SR

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where each group R may independently be hydrogen, $C_1\text{-}C_6$ alkyl or substituted $C_1\text{-}C_6$ alkyl, and

Y may be 0, 1 or 2 oxygen atoms, or NR where R may be H, OH, OR or a carbon atom, where R may be C_1 - C_6 alkyl or substituted C_1 - C_6 alkyl.

Q represents

$$R_{5}$$
 or R_{5}

wherein m is an integer from 1 to 4; n is an integer from 1 to 8; and R⁴ and R⁵ each independently represents hydrogen, unsubstituted or substituted C₁-C₁₀ alkyl, an unsaturated hydrocarbon chain of up to ten carbon atoms comprising one or more carbon-carbon double bonds, C₆ or C₁₀ aryl, a 5- to 10-membered heterocyclic group, C₁-C₁₀ alkoxy, C₁-C₁₀ thioalkoxy, hydroxyl, halo, cyano, nitro, amino, amido, (C₁-C₁₀ alkyl)carbonyloxy, (C₁-C₁₀ alkoxy)carbonyl, (C₁-C₁₀ alkyl)carbonyl, (C₁-C₁₀ alkyl)suflonylamino, aminosulfonyl, C₁-C₁₀ alkylsulfinyl, C₁-C₁₀ alkylsulfonyl, or a saturated or unsaturated C₃-C₁₂ hydrocarbon chain interrupted by O, S, NR, CO, C(NR), N(R)SO₂, SO₂N(R), N(R)C(O)O, OC(O)N(R), N(R)C(O)N(R), OC(O), C(O)O, OSO₂, SO₂O or OC(O)O where R is as defined above and the saturated or unsaturated hydrocarbon chain is optionally substituted as defined above;

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or a pharmaceutically acceptable salt thereof.

2. A compound as claimed in claim 1, in which the compounds are of general formula (I) have the formula (Ia)

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$$R_1$$
 R_2
 R_3
 R_3
 R_4
 R_4

3. A compound as claimed in claim 1, in which the compounds are of general formula (Ib)

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$$R_1$$
 R_2
 R_3
 R_2
 R_3
 R_4
 R_5
 R_5
 R_5
 R_5

4. A compound of claim 1, in which the compounds are of general formula (A)

 R_4 (A) (A)

in which V and W are as follows:

a single carbon-carbon bond,

V is CR and W is N, saturated or unsaturated

V is N and W is CR, saturated or unsaturated

a linkage of the form VW or WV = RRC-O or RRC-S.

wherein V and/or W may be optionally substituted (C_1-C_6) alkyl, C_6 aryl or heterocycle, and in which each group R is independently defined.

15 5. A compound of claim 1, in which the compounds are of general formula (B1)

in which n is equal to zero, one or two, and Z is a two-atom linkage of varying combinations of atoms of C, O, N, S, SO, SO₂, and in which each group R is independently defined.

6. A compound of claim 1, in which the compounds are of general formula (B2)

$$R_1R_2N$$
 (B2)

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in which n is equal to zero, one or two, Y is no atom present, O or O_2 or NR and Z = CR or N; or

in which n is equal to zero, one or two and X = NHOH, OH, NROR, CRROH;

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and Z is a one atom linkage of N or C, or a two-atom linkage of varying combinations of atoms of C, O, N, S, SO, SO₂, and in which each group R is independently defined.

7. A compound of claim 1, in which the compounds are of general formula (C)

$$R_{4} N R_{5}$$
(C)

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in which Y is equal to no atom, O or O_2 or NR and n is equal to zero, one or two and X is equal to NHOH, OH, NROR, CRROH, and in which each group R is independently defined.

- 5 8. A compound as claimed in claim 1, in which R² and R³ are both Hydrogen.
 - 9. A compound as claimed in claim 1, in which R^2 is methyl (CH₃) and R^3 is Hydrogen.
- 10 10. A compound as claimed in claim 1, in which R² is Hydrogen and R³ is methyl (CH₃).
 - 11. A compound as claimed in claim 1, in which R² and R³ are both methyl (CH₃).
- 15 12. A compound as claimed in claim 1, in which R^1 is $(C_6$ or $C_{10})$ aryl, optionally substituted by halo, (C_1-C_{10}) alkoxy, or by (C_1-C_{10}) alkylamino.
 - 13. A compound as claimed in claim 1, in which X is -OH, $-OC_2H_5$, $-OCH_3$, or NHOH.
 - 14. A compound as claimed in claim 1, in which Y is represented by one or two oxygen atoms.
- 15. A compound as claimed in claim 1, in which R² and R³ are both Hydrogen
 (H), Y is equal to zero oxygen atoms, and n is equal to 1, R¹ is one of

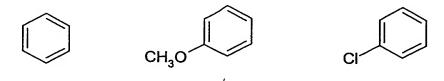


and X is one of -OH, -OCH₃, -OC₂H₅ or NHOH.

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16. A compound as claimed in claim 1, in which R^2 and R^3 are both Hydrogen (H), Y is equal to one oxygen atom, and n is equal to 1, R^1 is one of



and X is one of -OH, -CH₃, -OC₂H₅ or NHOH.

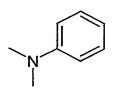
17 A commound on element 1 1 1 1 1 1 2 2

17. A compound as claimed in claim 1, in which R² and R³ are both Hydrogen (H), Y is equal to two oxygen atoms and n is equal to 1, R¹ is one of



and X is one of -OH, -CH₃, -OC₂H₅ or NHOH.

18. A compound as claimed in claim 1, in which R^2 and R^3 are both methyl (CH₃), Y is equal to zero oxygen atoms, and n is equal to zero, R^1 is



- and X may be $-OCH_3$, $-OC_2H_5$ or -OH.
 - 19. A compound as claimed in claim 1 which is:
 - 6-Phenylsulfanyl-hexa-2,4-dienoic acid (6a)
- 20 6-(4-Chloro-phenylsulfanyl)-hexa-2,4-dienoic acid methyl ester (6b)
 - 6-Phenylsulfanyl-hexa-2,4-dienoic acid methyl ester (6c)
 - 6-(4-Dimethylamino-phenylsulfanyl)-hexa-2,4-dienoic acid methyl ester (6d)

- 6-(4-Methoxy-phenylsulfanyl)-hexa-2,4-dienoic acid methyl ester (6e)
- 6-(4-Chloro-phenylsulfanyl)-hexa-2,4-dienoic acid hydroxyamide (7b)
- 6-(4-Dimethylamino-phenylsulfanyl)-hexa-2,4-dienoic acid hydroxyamide (7c)
- 6-Phenylsulfinyl-hexa-2,4-dienoic acid methyl ester (8a)
- 5 6-(4-Chloro-benzenesulfinyl)-hexa-2,4-dienoic acid methyl ester (8b)
 - 6-(4-Methoxy-benzenesulfinyl)-hexa-2,4-dienoic acid methyl ester (8c)
 - 6-Benzenesulfinyl-hexa-2,4-dienoic acid (8d)
 - 6-(4-Chloro-benzenesulfinyl)-hexa-2,4-dienoic acid hydroxyamide (9a)
- 6-(4-Methoxy-benzenesulfinyl)-hexa-2,4-dienoic acid hydroxyamide (9b)
 - 6-Benzenesulfonyl-hexa-2,4-dienoic acid (10a)
 - 6-Benzenesulfonyl-hexa-2,4-dienoic acid methyl ester (10b)
 - 6-Benzenesulfonyl-hexa-2,4-dienoic acid hydroxyamide (11a)
 - 6-(Naphthalen-2-ylsulfanyl)-hexa-2,4-dienoic acid methyl ester (13b)
- 15 6-(Naphthalen-2-ylsulfanyl)-hexa-2,4-dienoic acid hydroxyamide (14a)
 - 4-(4-Dimethylamino-phenylsulfanyl)-2-methyl-pent-2-enoic acid methyl ester (21b)
 - 6-(4-Dimethylamino-phenylsulfanyl)-4-methyl-hepta-2,4-dienoic acid ethyl ester (24c)
 - 6-(4-Dimethylamino-phenylsulfanyl)-4-methyl-hepta-2,4-dienoic acid hydroxyamide
- 20 (25c)
 - 6-(4-Chloro-phenylsulfanyl)-hexanoic acid methyl ester (28b)
 - 7-(4-Chloro-phenylsulfanyl)-heptanoic acid ethyl ester (28c)
 - 6-(4-Amino-phenylsulfanyl)-hexanoic acid methyl ester (28d)
 - 6-(4-Dimethylamino-phenylsulfanyl)-hexanoic acid methyl ester (28e)
- 6-(4-((4-Chlorobenzyl)-methylamino)-phenylsulfanyl)-hexanoic acid methyl ester (28f)
 - 6-(4-(4-Chlorobenzenesulfonylamino)-phenylsulfanyl)-hexanoic acid methyl ester (28g)
 - 6-(4-Bromo-phenylylsulfanyl)-hexanoic acid methyl ester (28h)
- 30 6-(4'-Chloro-biphenyl-4-ylsulfanyl)-hexanoic acid methyl ester (28i)
 - 6-(4-Chloro-phenylsulfanyl)-hexanoic acid hydroxyamide (29b)
 - 6-(4-Dimethylamino-phenylsulfanyl)-hexanoic acid hydroxamide (29c)

ethyl

- 6-(4-(4-Chlorobenzenesulfonylamino)-phenylsulfanyl)-hexanoic acid hydroxamide (29g)
- 6-(4'-Chloro-biphenyl-4-ylsulfanyl)-hexanoic acid hydroxamide (29i)
- 6-(4-Chloro-benzenesulfinyl)-hexanoic acid methyl ester (30b)
- 5 7-(4-Chloro-benzenesulfinyl)-heptanoic acid ethyl ester (30c)
 - 6-(4-Dimethylamino-benzenesulfinyl)-hexanoic acid methyl ester (30e)
 - 6-(4-((4-Chlorobenzyl)-methylamino)-benzenesulfinyl)-hexanoic acid methyl ester (30f)
 - 6-(4'-Chloro-biphenyl-4-ylsulfinyl)-hexanoic acid methyl ester (30i)
- 10 6-(4-Chloro-benzenesulfinyl)-hexanoic acid hydroxyamide (31a)
 - 7-(4-Chloro-benzenesulfinyl)-heptanoic acid hydroxyamide (31c)
 - 6-(4-Dimethylamino-benzenesulfinyl)-hexanoic acid hydroxyamide (31e)
 - 6-(4-((4-Chlorobenzyl)-methylamino)-benzenesulfinyl)-hexanoic acid hydroxamide (31f)
- 6-(4'-Chloro-biphenyl-4-sulfinyl)-hexanoic acid hydroxyamide (31i)
 (2E,4E)-5-(5-Dimethylamino-benzo[b]thiophen-2-yl)-penta-2,4-dienoic acid

ester (41a)

- (2E,4E)-5-(5-Dimethylaminobenzo[b]thiophen-2-yl)-penta-2,4-dienoic acid hydroxamide (42a)
- 20 (E)-3-(3-(4-Dimethylamino-phenylsulfanyl)-phenyl)-acrylic acid ethyl ester (51a. (E)-3-(3-(4-Dimethylamino-phenylsulfanyl)-phenyl)-N-hydroxy-acrylamide (52a)
 - 20. 4-(4-Dimethylamino-phenylsulfanyl)-2-methyl- pent-2-en-1-ol (22b)
- 25 21. A process for the preparation of a compound of general formula (II), comprising the addition of a compound of general formula (III),

$$W \xrightarrow{R_3 \atop R_2} Q OR$$

(III)

optionally followed by hydrolysis, or oxidation then hydrolysis, where W is a leaving group.

22. A process as claimed in claim 21, in which the compound of general formula (II) is a compound of general formula (5) and the compound of general formula (III) is a compound of general formula (4),

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optionally followed by hydrolysis, or oxidation then hydrolysis.

23. A process as claimed in claim 21, in which the compound of general formula (II) is a compound of general formula (20) and the compound of general formula (III) is a compound of general formula (17),

26. A process for the preparation of a compound of general formula (I), comprising the addition of a compound of general formula (IV) to general formula (Va) or (Vb),

$$\begin{array}{c|c}
R_6 & & & \\
R_7 & R_8
\end{array}$$
(IV)

$$R_{12}$$
 R_{11} R_{10} R_{10} R_{12} R_{11} R_{11} R_{11} R_{12} R_{11} R_{11} R_{12} R_{11}

$$R_{12}O$$
 $R_{12}O$
 R_{11}
 $R_{12}O$
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 $R_{12}O$
 $R_{12}O$
 $R_{12}O$

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(Vb)

(Va)

optionally followed by hydrolysis, or oxidation then hydrolysis.

15 27. A process as claimed in claim 26, in which the compound of general formula (IV) is a compound of general formula (39), and the compound of general formula (Vb) is a compound of general formula (40)

optionally followed by hydrolysis, or oxidation then hydrolysis.

5 28. A process as claimed in claim 26, in which the compound of general formula (IV) is a compound of general formula (49) oxidised to the corresponding aldehyde,

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and the compound of general formula (Va) is a compound of general formula (50)

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optionally followed by hydrolysis, or oxidation then hydrolysis.

- 29. A pharmaceutical composition comprising a compound of general formula (I) as defined in any preceding claim, and optionally a pharmaceutically acceptable adjuvant and/or diluent.
- 30. A compound of general formula (I) as defined in any preceding claim for use in medicine.

31. A method of treatment of an individual suffering from a disease condition, the method comprising administering to the individual a therapeutically effective amount of a compound of general formula (I) as defined in any preceding claim.

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32. A method of inhibition of histone deacetylase activity in an individual suffering from a disease condition, the method comprising administering to the individual a therapeutically effective amount of a compound of general formula (I) as defined in any preceding claim.

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33. The use of a compound of general formula (I) as defined in any preceding claim in the manufacture of a medicament for the treatment of cancer, including breast cancer, colon cancer, colorectal cancer, esophageal cancer, glioma, lung small and non-small cell cancers, leukaemia neuroblastoma, prostate cancer, thoracic cancer, melanoma, ovarian cancer, cervical cancer and renal cancer; cardiac hypertrophy, as well as haematological disorders including hemoglobinopathies, thalessmia, and sickle cell anemia, auto-immune diseases, such as arthritis, Huntington's disease, and neurological conditions, such as Alzheimer's disease, and genetic-related metabolic disorders, such as cystic fibrosis, peroxisome biogenesis disorders, adrenoleukodystrophy, stimulating hematopoietic cells ex vivo, ameliorating protozoal parasitic infection, accelerating wound healing and protecting hair follicles.